

DETAILED ACTION

Applicant's amendment of claims 25, 26, 29, 30 and the addition of new claims 42-45, in the paper of 3/14/2008, is acknowledged. Claims 25, 26 and 29-45 remain at issue and are present for examination.

Applicants' arguments filed on 3/14/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 25, 26, 29 and 30 are objected to because of the following informalities: The recitation in claims 25, 26, 29 and 30, which states "when cultured in IGF-1" is considered awkward. It is suggested that this be amended to more accurately reflect applicants disclosed experiments (i.e. cultured in the presence of IGF-1, etc...).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 26, 29-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Previously claims 25, 26, 29-41 were rejected under this statute because the newly added recitation of "the majority of which mature into oligodendrocytes" is not supported by applicant's specification at the time of filing and is thus considered new matter. Applicants statement of support at page 5, lines 17-22; page 7, lines 12-18; page 13, lines 30-32; page 11, lines 10-13; page 20, lines 11-15; page 21, lines 21-25; page 22, lines 11-12; page 23, lines 13-15 and 18-22; and Figure 4, as well as the rest of applicants specification has been considered, however, it remains that support for this newly amended recitation and the claimed genus of cells could not be found (See also above 112 second paragraph rejection).

In response to this previous rejection, applicants have amended the claims and submit that the claims are fully supported by the disclosure for reasons noted in applicants support for applicant's most recent amendment.

This complete argument is acknowledged, however, continues to be found nonpersuasive on the basis that while applicants may have support for some specific embodiments of the recited claims, applicants do not have support for claimed genus relative to those preparations wherein the majority of cells in the enriched or purified preparation mature into oligodendrocytes when cultured in IGF-1".

This lack of support of applicant's newly amended claims is additionally rejected on the basis that applicants do not have support for the majority of cells mature into oligodendrocytes when cultured in IGF-1. Applicants submission of support for "culturing in IGF-1" in Figure 4, is acknowledged, however, it appears that Figure 4 actually indicates "culturing in the presence of "5%FBS/IGF-1", not "cultured in IGF-1".

Claims 42-45 are additionally rejected as containing additional subject matter which is not supported by applicant's specification at the time of filing and is thus considered new matter. Specifically applicant recitation to "at least 59.5% of cells" is not supported by applicant's specification at the time of filing and is thus considered new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26 and 29-41 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

This rejection which was stated in the previous office action as it applied to claims 25, 26 and 29-41. In response to the rejection applicants have amended claims 25, 26, 29, 30 and added new claims 42-45 and continue to traverse the rejection as it applies to the newly amended claims.

For applicants convenience the original rejection is repeated herein:

Rao et al. teach an isolated, pure (enriched or purified) and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and differentiation into oligodendrocytes and astrocytes and methods of generating, isolating and culturing such oligodendrocyte-astrocyte precursor cells. The specific pure homogeneous population of cells isolated by Rao et al. is illustrated in Figure 1 (See specifically cell type -14, and the supporting text) and while Rao et al. specifically teach as an example said pure (enriched or purified) homogeneous preparation of cells as isolated from rat, Rao et al. point out that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. Thus, Rao et al. anticipates those claims to an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, the majority of which mature into oligodendrocytes, wherein an oligodendrocyte specific promoter (CNP2) is transcriptionally active in the oligodendrocyte progenitor cells..

The preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the

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enriched or purified preparation. This is evidenced by the reference Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994, see applicants IDS) who teach the differential cellular and temporal regulation of the 2',3'-cyclic nucleotide 3'-phosphodiesterase gene (CNP) and teach that the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter is transcriptionally active in oligodendrocytes, Schwann cells and many additional tissues and appears before the appearance of mature oligodendrocytes, in oligodendrocyte precursor cells early in brain development (See page 1365-1367, Figures 4 and 5 and supporting text).

Claims 25, 26 and 30, which are drawn to the preparation of oligodendrocyte progenitor cells of claim 29 are included in this rejection because these product-by-process like limitations ("from a post-natal human" for claim 25 and "from an adult human" for claim 26, fetal human) do not change the oligodendrocyte progenitor cells of claim 29. Rao further teaches that a better understanding of a number of tumors and other diseases in humans could be facilitated by a better understanding of these cell types and the ability to isolate and grow these mammalian cells in vitro, which allows for the possibility of using such stem cells to treat neurological disorders in mammals, particularly humans. Further, such mammalian neuroepithelial stem cells can be used therapeutically for treatment of certain diseases, e.g. Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. Moreover, such cells can still further be used for the discovery of genes and drugs that are useful for treating certain of these diseases.

One of ordinary skill in the art at the time of filing would have been motivated to use the methods taught by Rao et al. to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells from humans so that these pure cell preparations could be used to treat neurological disorders in humans, such as Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. This motivation is suggested by Rao et al. and the reasonable expectation of success comes from the results of Rao et al. who successfully isolated such an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat.

Applicants continue to give applicants interpretation of the '996 patent and applicants submit the '996 patent discloses multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells. In particular, applicants submit that after differentiation, in Example 14, the proportion of differentiated cells was 30% oligodendrocytes, 50% astrocytes, and 20% A2B5⁺ cells.

Applicants submit that similarly, Example 15 of the '996 patent, the A2B5⁺ cells predominantly differentiate into cells with a type-2 astrocyte phenotype and this is entirely consistent with the previously submitted Second Declaration of Mahendra S. Rao, M.D., Ph.D. Under 37 C.F.R. § 1.132 ("Second Rao Declaration").

Applicants submit that this bias of the '996 patent's astrocyte/oligodendrocyte progenitor to differentiate to astrocytes clearly distinguishes them from the presently claimed oligodendrocyte progenitor cells, the majority of which mature into oligodendrocytes.

Applicants again point out that it is important to note that multiple pathways to generate post-mitotic, mature oligodendrocytes, have been described and applicants again summarize these as they have previously done.

Applicants focus on those comments of the previous Examiner's Answer which states that the previous claims are anticipated by Examples 7 and 15 of the '996 patent, as according to the PTO, these examples must produce an intermediate between the '996 patent's oligodendrocyte-astrocyte precursor cells and fully differentiated cells. Applicants submit that the PTO particularly relies on Example 7's mention of cells that appeared to have a different morphology than the oligodendrocyte type-2 astrocyte progenitors or mature oligodendrocytes in asserting anticipation. Applicants disagree with this argument on two basis. Firstly, applicants continue to submit that these examples involve work with rat cells - not human cells. This response is recognized, however, not found persuasive on the basis that as previously stated, those claims drawn to the preparation of oligodendrocyte progenitor cells are included in this rejection because these product-by-process like limitations ("from a post-natal human" for claim 25 and "from an adult human" for claim 26) do not change the oligodendrocyte progenitor cells of claim 29. Further applicants are reminded that the current rejection is a 102/103 type rejection and while the origin of the taught by Rao et al. may be rat, applicants is reminded that one of skill in the art would be motivated to isolate the same cell population from human sources.

Secondly applicants continue to submit that the mention of cells having a morphology that is different than the oligodendrocyte type-2 astrocyte progenitors or

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mature oligodendrocytes does not mean that those additional cells are the claimed oligodendrocyte progenitor cells. Applicants submit that the PTO's point is entirely speculative and is contrary to what Dr. Rao said in his second declaration and in taking this position, the previous Examiner's Answer is impermissibly ignoring the testimony of Dr. Rao who is in a far better position to know what cell types his work made and did not make. Applicants argument is again acknowledged, however, not found persuasive on the basis that as previously stated it is a reasonable and logical assertion that the cell type which is at the heart of applicants invention is an intermediate between the cell type 14 and 18 of Rao et al. and it must have existed in the preparations of Examples 15 and 7. Applicants have submitted that there is no evidence of such in the presentation of Dr. Rao's declaration, however, this is contrary to the teaching of Rao et al. as presented previously and below.

Applicants submit that given Rao's clear teaching that his oligodendrocyte-astrocyte precursor cells have an astrocytic bias, it is not apparent how these cells can be regarded as the same as the claimed enriched or purified preparation from which a majority of the cells mature into oligodendrocytes. In any event, applicants submit that the claims have been amended to recite the conditions under which a majority of the cells in the enriched or purified preparation can mature into oligodendrocytes (i.e. cultured in IGF-1). Since neither these conditions, let alone the result that a majority of the cells of the enriched or purified preparation mature into oligodendrocytes are taught by Rao, this reference can hardly be said to teach or render obvious the claimed invention.

Applicant's complete argument and amendment of the claims, continues to be acknowledged and has been carefully considered, however, continues to be found nonpersuasive for the reasons previously made of record in the previous office actions and the previous examiners answer and for those reasons discussed above and below.

It continues that applicants have amended the claims to recite "an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, "wherein the majority of cells in the enriched or purified preparation mature into oligodendrocytes when cultured in IGF-1..."

As previously stated if one considers that applicants claims are directed to an oligodendrocyte-specified progenitor cell which is "unipotential" such that it only gives rise to oligodendrocyte cells and not to other types of cells, such as astrocytes, then this "further specified oligodendrocyte-specified progenitor cell" continues to be anticipated by Rao et al. in its preparations of examples 15 and 7. Each of these example preparations start with NEP-derived A2B5+ cells and allow these progenitors to develop to oligodendrocytes. Thus, the NEP cells differentiated to cell type 14 (as per Figure 1) and further differentiated to cell type 18 (as per Figure 1). Thus an intermediate between the cell type 14 and 18 must have existed in the preparations of Examples 15 and 7.

Previously relative to this argument, applicants submitted that Dr. Rao is not aware of any evidence that the astrocyte/oligodendrocyte precursor cells of the '996 patent generated mature oligodendrocytes by way of an intermediate oligodendrocyte-specific precursor and applicants further presented Gregori et al., J Neurosci. 22(1):248-

256 (2002) as suggesting that the '996 patent describes a glial progenitor that gives rise to a more restricted astrocyte/oligodendrocyte precursor that still directly makes predominantly astrocytes and a small minority of oligodendrocytes. Thus, applicants submitted that cells in the '996 patent's pathway to oligodendrocyte production are bi-potential astrocyte/oligodendrocyte progenitor cells that have strong astrocytic bias. Applicants continue to submit that these cell types are very different from the claimed oligodendrocyte-specified progenitor cells of the present application.

As in the previous responses to this argument, if one considers that the claimed progenitor cell must be unipotential, such that it only differentiated into an oligodendrocyte cell, (that is an intermediate between cell type 14 and cell type 18) then contrary to the declaration of Dr. Rao, there is evidence of the existence of such a cell type. This evidence is found in Example 7 of the Rao et al. patent.

As demonstrated in example 7 of Rao et al., NEP cells grown on fibronectin in NEP medium for 5 days according to the procedure of Example 1 were harvested by trypsinization and replated on laminin-coated plates in neuroepithelial culture (NEP) medium without the addition of CEE for 5-10 days. Differentiating NEP cells were then labeled, according to the procedure of Example 4, with markers previously identified as being expressed on oligodendrocytes and their precursors: A2B5, GalC, O1, and O4. Three days after replating NEP cells, a subset of the cells began to express A2B5 immunoreactivity. A2B5 immunoreactive cells initially did not express detectable levels of GalC, O4, and O1 immunoreactivity. These cells correspond to the Figure 1, cell type 14. After an additional three days in culture, however, "GalC immunoreactive cells

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could be seen, which cells also expressed A2B5 immunoreactivity". Such cells appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes. Longer periods in culture, however, allowed more mature-looking oligodendrocytes with a small body and extensive processes to develop. These cells expressed O1 and GalC immunoreactivity, markers characteristic of differentiated oligodendrocytes. These cells which "appeared flattened and did not have the characteristic morphology of oligodendrocyte-type 2-astrocyte (O2A) progenitors or mature oligodendrocytes" are evidence of the existence of an intermediate between cell type 14 and cell type 18 of Figure 1. As stated by Rao et al., the pattern of antigen expression further suggests the existence of a dividing oligodendrocyte precursor that subsequently generates oligodendrocytes, as has been described from spinal cord cultures from older embryos. It is this identified cell type that continues to anticipate applicants claimed cells.

For these reasons, claims 25, 26 and 29-45 remain rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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6/18/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652